

Bond University
Research Repository



The Impact of Acupuncture on Neurological Recovery in Spinal Cord Injury A Systematic Review and Meta-Analysis

Ma, Ruijie; Liu, Xin; Clark, Justin; Williams, Gail M; Doi, Suhail A R

Published in:
Journal of Neurotrauma

DOI:
[10.1089/neu.2014.3866](https://doi.org/10.1089/neu.2014.3866)

Published: 15/12/2015

Document Version:
Peer reviewed version

[Link to publication in Bond University research repository.](#)

Recommended citation(APA):

Ma, R., Liu, X., Clark, J., Williams, G. M., & Doi, S. A. R. (2015). The Impact of Acupuncture on Neurological Recovery in Spinal Cord Injury: A Systematic Review and Meta-Analysis. *Journal of Neurotrauma*, 32(24), 1943-1957. <https://doi.org/10.1089/neu.2014.3866>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

For more information, or if you believe that this document breaches copyright, please contact the Bond University research repository coordinator.

The Impact of Acupuncture on Neurological Recovery in Spinal Cord Injury: A Systematic Review and Meta-analysis

Ruijie Ma^{1,2*}, Xin Liu^{1,3,4}, Justin Clark⁵, Gail M. Williams², Suhail A. Doi⁶

¹The Third Clinical School, Zhejiang Chinese Medical University, Hangzhou, China

²School of Population Health, The University of Queensland Brisbane, Australia

³Wuhan Sport University, Wuhan, China

⁴School of Medicine, University of Queensland, Brisbane, Australia

⁵Centre for Research into Evidence Based Practice, Bond University, Gold Coast, Australia

⁶Research School of Population Health, Australian National University, Canberra, Australia

Ruijie Ma, PhD, Associate Professor

The Third Clinical School, Zhejiang Chinese Medical University, Hangzhou, China

School of Public Health, University of Queensland, Brisbane, Australia

Email: maria7878@sina.com

Tel: +86 15990051481

Xin Liu, PhD

The Third Clinical School, Zhejiang Chinese Medical University, Hangzhou, China

School of Medicine, University of Queensland, Brisbane, Australia

Wuhan Sport University, Wuhan, China

Email: xin.liu@uqconnect.edu.au

Tel: 0423677118

Justin Clark, BA, Lib Tech

Centre for Research into evidence Based Practice, Bond University, Gold Coast, Australia

Email: jclark@bond.edu.au

Tel: +614 08951782

Gail M. Williams, PhD, Professor

School of Public Health, University of Queensland, Brisbane, Australia

Email: g.williams@sph.uq.edu.au

Tel: +614 12168914

Suhail A. Doi, PhD

Research School of Population Health, Australian National University, Canberra, Australia

Email: sardoi@gmx.net

Tel: +61 404181134

*** Corresponding author:**

Ruijie Ma, PhD, Associate Professor

School of Public Health,

University of Queensland

Herston road, Brisbane, QLD 4006, Australia

Tel: +614 16686465/ +86 15990051481

E-mail:maruijie7878@gmail.com

Abstract

Spinal cord injury (SCI) has become a significant social and economic burden for patients and their families. The effect of acupuncture on neurological recovery in individuals with SCI remains inconclusive despite previous studies and meta-analyses. The aim of the current study was to perform a more rigorous systematic review and bias adjusted meta-analysis of studies so that the overall impact of acupuncture on neurological recovery in SCI can be determined. Randomised controlled trials only were included and were searched for in seven databases through to August 2014. Four key outcomes were assessed: Neurological recovery, motor function, sensory function and functional recovery. Several statistical approaches were compared, models were tested for robustness using sensitivity analysis and results are presented as weighted mean difference (WMD) or standardized mean difference (SMD) for continuous outcomes and relative risk (RR) for binary outcomes. The included studies' susceptibility to bias was also assessed. A total of 12 studies were included after exclusions were applied. Heterogeneity was evident among the studies included. Pooled analyses showed that acupuncture may have a beneficial effect on neurological recovery (RRs: 1.28, 95% CI: 1.12 – 1.50), motor function (WMD: 6.86, 95% CI: 0.41 – 13.31) and functional recovery (SMD: 0.88, 95% CI: 0.56 – 1.21) and all statistical approaches concurred. Sensitivity analyses suggested that the smaller studies (sample size <30), those with acute disease and studies that used varying acupuncture sessions demonstrated a larger magnitude of effect. However, studies were generally of poor quality and publication bias favouring positive studies was evident. Therefore, the benefit of acupuncture we report is by no means definitive and well-designed future studies are recommended to confirm this.

Key words: meta-analysis; SCI; systematic review; acupuncture

1 Introduction

Today, SCI and its secondary complications have become a significant social and economic burden for the health care system and patient families. It is estimated that the annual incidence of spinal cord injury (SCI), excluding those who die at the scene of the accident, is approximately 40 cases per million population in the U. S. or approximately 12,500 new cases each year. The average yearly health care and living expenses costs an average of USD 6,661,632.9 in the first year and USD 97,997.41 in the each subsequent year which did not include any indirect costs such as losses in wages, fringe benefits and productivity which average USD 70,849 per year in November 2013 in the US.¹ An Australian study predicted that population growth and aging, and increasing rates of SCI in the elderly will have profound effects on the expected number of SCI patients and their case mix. It also predicted a 143% increase in the number of cases of incomplete tetraplegia, from 88 cases per annum in 1997 to 214 cases per annum in 2021.²

Although almost all people living with SCI show some recovery of motor and sensory function below the initial spinal injury level, spontaneous recovery in patients with complete-motor SCI is quite limited and predictable.³ Nevertheless there have been reports of favourable outcomes following treatment options such as surgery,⁴ pharmacological interventions,⁵ rehabilitation⁶ and alternative medicine approaches such as acupuncture.⁷⁻¹⁰ A review by Dorsher concluded that use of electroacupuncture in acute SCI may significantly improve long-term neurologic recovery from these injuries with essentially no risk¹¹. Acupuncture has also been shown to improve neurological function in individuals with chronic SCI, and help with management with chronic pain associated with these injuries.¹¹ However, the latter review did not systematically evaluate the available evidence.

In the last 5 years, two systematic reviews (including meta-analyses) examining acupuncture for SCI have been published.^{10, 12} One review based on 7 randomized control

trials (RCTs) conducted in China suggested that acupuncture is effective for functional recovery and bladder dysfunction in SCI. This review was limited to studies only retrieved from the database of the China National Knowledge Infrastructure (CNKI: www.cnki.co.kr) till May 2008 and 3 more recent studies were therefore not included.¹³⁻¹⁵

A more recent review has been undertaken by Heo and colleagues¹² that included 16 studies (8 for functional recovery from SCI, 6 for bladder dysfunction and 2 for pain control) based on a search till December 2011. Their systematic review and meta-analysis showed positive results for the use of acupuncture combined with conventional treatment for functional deficits and bladder dysfunction. However, the evidence generated through this review did not consider the impact of the methodological aspects of included studies and thus potential biases on the pooled outcome estimates. This is of particular importance in the complementary medicine literature given the lower quality of evidence in these studies.

In the current study, we aimed to improve on previous meta-analyses by including more recent studies, rigorously assessing quality of the randomized controlled trials and using bias adjusted methods in addition to conventional methods to derive pooled estimates of effect.

2 Methods

2.1 Data sources and eligibility criteria

A systematic search of the literature was conducted in PubMed, Cochrane (CENTRAL), Embase, CINAHL, AMED, SinoMed and the Chinese National Knowledge Infrastructure (CNKI). Citations that included both acupuncture and spinal cord injury until August 2014 were retrieved. The following search terms were used individually or combined for abstract retrieval: acupuncture, acupuncture therapy, spine, vertebral, spinal, wounds and injuries,

trauma, recovery of function, neurological, motor, score, and scale. Controlled vocabulary terms (e.g. MeSH terms) were also used for each of the databases in the Chinese and English languages. The search strategy was adjusted for each database. In addition, the bibliographies of relevant systematic reviews and clinical guidelines were manually searched.

The inclusion of studies was limited to randomised controlled trials (RCTs) reporting the prospective use of the acupuncture interventions in study participants who suffered from spinal cord injury (SCI). All trials selected were those that focused on functional recovery, while those that only reported complications such as bladder dysfunction or pain were excluded. This review included parallel group RCTs that assessed the efficacy of acupuncture regardless of blinding, or the type of control comparison.

Our study mainly considered needle acupuncture as the intervention of interest which included manual acupuncture, electro-acupuncture, auricular acupuncture and acupoint injection. Laser acupuncture, acupressure, and moxibustion were excluded. Studies on complications, prospective non-randomized studies, duplicate publications, studies which used acupuncture in both arms and studies without extractable data for analysis were also excluded.

2.2 Data extraction and quality assessment

Data extracted for each study is summarized in the data extraction table (see Tables 1 and 2). The data abstracted included the characteristics of each study, including the characteristics of included subjects (such as mean age, gender, type of injury, source of recruitment, eligibility), description of the acupuncture intervention and of the control group, SCI level, SCI severity was measured in the study at baseline using the American Spinal

Injury Association impairment grade (AIS grade) classified as A (no motor or sensory function) to E (normal motor and sensory function) and duration of follow-up.

2.2 *Quality ranking*

The quality of each study was assessed using a specifically created methodological quality checklist modified from several sources including the GRADE guidelines and Cochrane Collaboration's tool for assessing risk of bias.^{16, 17} Questions assessed the study design, selection, information, confounding, and analytical biases (see Table 3). The maximum score was 23 and we considered studies scoring 0-7 points to be low quality, 8-16 points to be moderate quality and 17-23 points to be high quality. Quality items were weighted equally and in general one point was assigned for a safeguard present and zero otherwise. The quality rank for each study was then calculated by summing the points awarded for each question and dividing this by the maximum within each meta-analysis performed, thereby having ranks that rescale downwards from 1 and resulting in study ranks between zero and one.

<Insert **Tables 1-3** here>

2.3 *Outcome measure and statistical analyses*

Outcomes

The assessment methodologies used in previous clinical studies fall into two main categories which are neurological and functional recovery. Neurological recovery is documented through the use of recovery scales that include measures of the grading of the motor and sensory abilities, using mainly the International Standards for Neurologic Classification of Spinal Cord Injury scale (ISNCSCI) also known as the American Spinal Injury Association (ASIA) scale which include motor, sensory and touch scales¹⁸. Because

the ASIA light touch scale does not necessarily correlate with subsequent sensory function accurately¹⁹, we pooled the data for the ASIA pin-prick scale for this meta-analysis.

While the objective neurological scores assess the remaining connections within the spinal cord, they do not assess the functional abilities of the patient, which also depend on motivation, rehabilitation, fitness and other factors affecting the individual. We thus also evaluated functional improvement through the subject's ability to perform activities of daily living (ADL) or equivalent. These tests focus on issues related to the rehabilitation of the patient, and may change independently of neurological outcomes or CNS connectivity; patients with the same neurological scores may therefore, have rather different functional abilities. Finally, we also assessed subjective physician assessment of "recovery" (yes/no).

Our measures of outcome therefore included four outcome measures two of which were the weighted or standardized mean difference in motor and sensory score between acupuncture and control groups at the end of follow-up, the third was the standardized mean difference in functional recovery. The fourth outcome was neurological recovery as a binary variable (yes/no) at the end of follow-up in each group from which the relative risk was computed.

Statistical analysis

The mean and standard deviation of the scores in each arm were used to compute effect sizes. Standard deviations were calculated from either the confidence intervals or the standard error and sample size when standard deviations were not given from individual reports. Three statistical models were used to pool data and included the conventional random effects (RE) model, the inverse variance heterogeneity (IVhet) model²⁰ and the quality effects (QE) model²¹. The quality scores were used to redistribute inverse variance weights based on relative study ranking of safe-guards used against bias using a quality-effects (QE) model.²²⁻

²⁴ Therefore, weight redistribution occurred in favour of the studies with higher methodological quality ranking, which contributed to a higher weighting of these studies towards the overall effect size.²² Heterogeneity was assessed by the Cochran's Q test, the I^2 index, and the Tau-squared statistic (τ^2), as well as through graphical evaluation of the forest plot. Heterogeneity was defined as a Cochran's Q test p -value of less than 0.1, or a τ^2 value of greater than zero.²⁵

A sensitivity analysis was conducted to determine the degree to which the main findings vary depending on the selection criteria of studies included in the meta-analysis. These selection criteria included publication year, study sample size, duration of the disease, severity of injury, control group interventions, sessions given and type of the outcome scales. The sensitivity analysis determined if these selection criteria had a substantial impact on the pooled standardized mean difference in functional recovery. The sensitivity analysis was limited to functional recovery because it had the largest number of studies.

Publication bias was examined by visual inspection of the funnel plot, but given that its visual appearance can be problematic, a *Doi plot* was also used to graphically evaluate publication bias²⁶. Effect estimates were considered statistically significant if the 95% confidence intervals did not include zero in the case of WMD or SMD and unity in the case of the RR²⁷⁻²⁹. The data were analysed using the MetaXL software version 2.0 for Windows (www.epigear.com).

3 Results

3.1 Search results

The computerized search strategy resulted in 3789 citations after duplications were removed. After screening of titles and abstracts, 54 potentially eligible articles were obtained

for full-text screening and of these 42 articles were excluded after a more detailed full text evaluation. Most of the articles excluded focused on the complications post spinal cord injury such as bladder dysfunction or pain. Additionally, studies which used acupuncture in both arms and duplicate publications were also excluded. Finally 12 studies (Figure 1) that reported on the effects of acupuncture on neurologic recovery after spinal cord injury were included for meta-analysis.^{13-15, 30-38}

<Insert **Fig. 1** here>

3.2 Study Characteristics

All 12 included studies were randomized controlled trials (see Tables 1 and 2). Control conditions in the reviewed studies included medications and rehabilitation for SCI). The acupuncture intervention period across all studies ranged between 30 days to 18 months. The interventions included manual acupuncture (insertion of needles into acupoints, followed by manual manipulation), electro-acupuncture (two needles are inserted as electrodes for passing an electric current and at least one of the needles is on an acupoint), auricular acupuncture (which may be effective for a long time with some seeds or pills (instead of needles) for acupressure) and acupoint injection (the injection at acupoints with a small amount of a drug, is a recent innovation of traditional acupuncture and aims to enhance and prolong the effect of stimulation of acupuncture points). For the main intervention, 6 studies used electro-acupuncture,^{13, 14, 30-34, 36} 2 studies used electro-acupuncture combined with auricular acupuncture,^{13, 32} 3 studies used manual acupuncture^{15, 35, 37} and 1 study used acupoint injection with Mecobalamin³⁸

The description of the acupoints (defined as a historically and empirically predefined location within the human body) selected were also different with 6 studies selecting jiaji points (jia;

lining ji; spine) which are points at the level of the spinous process of the vertebrae 0.5-1.0 cm from the midline on the cervical spine and back).^{14, 15, 34-36, 38} 5 studies selected points on the governor vessel (a prominent body meridian whose main pathway ascends within the spinal column).^{14, 30, 34, 35, 38} Ten studies selected acupoints on the limbs as the main points or as additional points^{13-15, 31-36} while only 3 studies did not use any acupoint on limbs.^{30, 37, 38}

The main advantage in using electroacupuncture is its capacity to set stimulation frequency and magnitude objectively and the electrical frequency used was reported to be 1-2hz³⁰, 20 Hz,³⁴ 60hz,³³ and 75 Hz with a pulse duration of 200 seconds.¹³ The magnitude of stimulation was set as either 10 V,¹³ or 3-5V³³ and the wave was described as a continuous wave³³ or a wave depending on paralysis type.³¹ The other 7 studies didn't describe any parameters of electroacupuncture that were used.^{14, 15, 32, 35-38} Each treatment session was usually 20-30 mins, once per day, 6-10 times over the course of the study.

There were 9 studies where acupuncture treatment combined rehabilitation therapy^{13, 30-33, 35, 37} and used the rehabilitation therapy as the control group. There were 2 studies where treatment combined rehabilitation therapy and medications as the control group.^{34, 38} Three studies used medications as the control group^{14, 15, 36} and another study selected conventional treatment and nursing as the control group.³⁵ In one study with 3 arms (two control arms) we selected traditional Chinese medicine decoction (this is the process by which herbs are boiled and the remaining liquid is used for health purposes) as the control group and we compared this to the acupuncture group.¹⁴

3.3 Participants

The included studies comprised 749 participants in total of whom 378 were given acupuncture treatment. Of the latter, 251 were given acupuncture treatment combined with

rehabilitation. In terms of the control subjects, rehabilitation was given to 198 participants while rehabilitation combined with medication was given to another 108 participants. Only 65 participants were given medication (herbs or western medicine) as the control intervention.^{14, 15, 36} There were 447 males and 206 females and another 96 participants from studies which did not report gender.

3.4 *Quality of the studies*

The quality assessment revealed that only one of the thirteen studies was high quality, and the remaining 12 studies were of moderate quality. The main quality defects in more than half of the studies were 1) inclusion/exclusion criteria not clearly described, 2) outcome assessors not blinded to the nature of intervention, 3) no records or control of concurrent interventions or exposures that could affect outcomes, and 4) intention-to-treat analyses not conducted for the outcome of interest.

3.5 *Quantitative synthesis*

Neurological recovery

Neurological recovery (subjective assessment by physician) increased by 28% in those receiving acupuncture (RR 1.28; 95% CI 1.12 – 1.50) in 5 studies^{31, 32, 34, 35 14} comprising 327 subjects. Studies were considered homogeneous ($I^2 = 26\%$; $p = 0.25$), and the QE model was used to pool the data. The RE and IVhet results concurred (Figure 2). The bias adjusted analysis included consideration of baseline severity of SCI. At baseline two studies reported an AIS grade of A – B^{13, 30}, one study reported an AIS grade of A – D³³, one study reported an AIS grade of C – D³⁶, one study reported an AIS grade of B – D³⁷.

<Insert **Fig. 2** here>

Motor score

The weighted mean difference (WMD) in motor score was 6.86 (95% CI 0.41 – 13.31) in 4 studies^{13, 32, 36, 38} using the QE model comprising 260 subjects which means that acupuncture can result (on average) in an improvement of 6.86 points in motor score. Studies were considered heterogeneous ($I^2 = 87\%$; $p = 0.00$). Results using the IVhet and RE models were similar. The score used across all studies pooled was the ASIA motor score. Only the IVhet model (WMD: 6.46, 95% CI: -0.16-13.08) demonstrated no statistical significance suggesting that without consideration of quality, the variance induced by the heterogeneity was large.

<Insert **Fig. 3** here>

Sensory score

The standardized mean difference in sensory score was 0.85 (95% CI 0 – 1.71) in 3 studies^{13, 32, 38} comprising 220 subjects and this was not statistically significant. Studies were considered heterogeneous ($I^2 = 87\%$; $p = 0.01$). The results of the QE model were similar to those of the IVhet model. While the RE model suggested statistical significance, but as RE models are known to underestimate the statistical error^{39, 40}, this is likely to have been overstated. All studies used the ASIA sensory score but it should be noted that the ASIA sensory scoring used in Wong (2003) was the total score of 112 for 28 dermatomes on each side while it was a total score of 32 for 8 dermatomes on each side used by Chen (2005) and Ye (2014). We reported the standardised mean difference here as the scales were not comparable.

<Insert **Fig. 4** here>

Functional improvement score

The standardized mean difference in functional improvement score was 0.88 (95% CI 0.56 – 1.21) in 7 studies^{13, 15, 32, 33, 36-38} comprising 422 subjects. Studies were considered heterogeneous ($I^2 = 87\%$; $p = 0.01$). There was no significant difference across statistical models. The main scores used were the functional independence measure (FIM) score (including the FIM self-complete score³² and FIM total score^{13, 33}), Barthel Index^{15, 38} and SCIM (spinal cord independence measure)³⁶ for activities of daily living (ADL) and Balance Subscale on FMA.³⁷ For ease of interpretation, we back-transformed the pooled effect size by multiplying it with the typical SD of the Spinal Cord Independence Measure (SCIM) scale.⁴¹ In terms of the SCIM scale, the converted WMD was 19.36 (95% CI 12.32-26.62) when the typical SD was taken to be 22.⁴² This suggests that on average the SCIM increases by almost 20 points with acupuncture. Given the scale ranges between 0-100, this represents an almost 20% greater functional recovery as assessed through the SCIM.

<Insert **Fig. 5** here>

Sensitivity analysis and publication bias

The smaller studies (sample size less than 30), those with acute SCI, and studies that used varying sessions demonstrated a larger magnitude of effect in functional recovery (see Table 4). Other sensitivity analyses based on publication year, severity of injury, control group interventions and type of the outcome scales did not demonstrate variation across groups. There was gross evidence of publication bias favouring positive studies across all outcomes. The Doi and funnel plots in **Fig. 6** demonstrated asymmetry suggesting that either there was gross heterogeneity such that small studies had systematically larger effects than larger

studies or maybe there was truly publication bias and studies with negative outcomes did not get published and were therefore missing.

<Insert **Table 4** here>

<Insert **Fig. 6** here>

4 Discussion

This meta-analysis demonstrates that acupuncture could have a beneficial effect on neurological recovery, motor function and functional recovery such as activities of daily living or independence. In sensitivity analyses, the smaller studies demonstrated a larger magnitude of effect in functional recovery (see Table 4). Additionally, the studies reporting acute SCI showed a larger magnitude of effect in functional recovery than those reporting chronic SCI. It should be noted that the chronic SCI will provide the most static functional baseline, because minimal spontaneous neurological improvement occurs after an individual has survived with SCI for a chronic period of time.⁴³ Number of sessions given also showed that studies that varied number of sessions demonstrated a larger magnitude of effect in functional recovery than those with a fixed number, which may imply a more rigorous protocol for the former.

Despite the positive results, several problems are evident with the studies we analysed. First, the funnel plot demonstrated asymmetry, suggesting potential publication bias where ‘negative’ studies were missing. The preferential publication of positive studies might be due to the rejection by journal editors of negative trials in this area, and seriously limits the validity of this meta-analysis. Second, the contents of the only English paper¹³ reported data that were called in question. They reported 5 out of 28 AIS A and 16 out of 22 AIS B recovering completely (=AIS E) in the acupuncture group and this seems too good to be true. This paper had the largest weight in the meta-analysis. Third, the paper of Chen 2005 does

not report baseline ASIA motor scores, hence we cannot establish that there were improvements for motor recovery. Fourth, many differences exist between affected individuals⁴³ including concomitant injuries and comorbidities and thus this makes it complicated to evaluate the effect of acupuncture per se in these clinical trials.^{4, 44-46} For example, studies have shown that in tetraplegia patients the ASIA motor score reveals relevant differences per spinal segment while in paraplegic patients there was no difference for the ASIA motor score between T2 and T8.⁴⁷ An outcome measure should have both precision and robustness, which means the overall findings are not significantly influenced by slight variations in treatment regimens, assessment procedures, or data analysis and this does not seem to be the case with the assessment scales used in these studies. Fifth, the quality of studies was poor overall and while differential quality was taken into account in the analysis, overall there were significant biases observed. Most prominent was the method of randomization where only five studies described the randomization procedures, while the remainder just mentioned that 'the patients were randomized into two groups' with no further information. Possibly some of these claimed RCTs were not appropriately randomised. Secondly, selection bias may arise from vague inclusion/exclusion criteria and control group selection. No sham acupuncture was used and participants in these trials are not blinded thus introducing information bias. In addition, participants in acupuncture trials might have enrolled because they have expectations for a benefit of acupuncture. No trial reported any drop-outs or withdrawals, or mentioned intention-to-treat analysis. In addition, only two trials reported the outcomes up to one year post injury, therefore the long-term effect of acupuncture could not be established. The sixth and final issue is that acupuncture is a systematic field which contains complex manipulation and different kinds of stimulation. In this review, the interventions included manual acupuncture, electro-acupuncture, auricular acupuncture and acupoint injection among which electro-acupuncture showed a competitive

advantage in 8 out of 12 (66.7%) included studies. One advantage of the widely used electroacupuncture in clinics is due to its fixed stimulation and ease of manipulation. However, acupoints selection and stimulation parameter of electroacupuncture varied among studies. Therefore it was difficult to estimate the correlation between the difference of acupuncture treatment and its therapeutic effectiveness. The recognized characteristics of acupuncture treatment such as acupoint, stimulation parameter and treatment sessions for SCI are still controversial. From our review of the evidence, we believe that using electroacupuncture on jiaji points may have a positive effect on functional recovery post spinal cord injury which is easy to manipulate using a stimulation parameter from 2 Hz to 20 Hz. Auricular acupuncture can be used as an auxiliary selection which cannot act as a replacement of body acupuncture for functional recovery.

On the positive side, our meta-analysis used a rigorous methodology, meticulously appraised study quality and incorporated these into the analyses. We also used three statistical models to overcome limitations inherent in the conventional models. The inclusion of quality scores in meta-analyses permits a better understanding of the variation between studies. The QE method seems to generate more conservative overall estimates when there is heterogeneity in the quality of studies. This is evident from the fact that the QE summary estimate had a higher variance and, consequently, a wider confidence interval than the RE summary estimate.²² Our specifically created methodological quality checklist was modified from several sources including the GRADE guidelines and Cochrane Collaboration's tool for assessing risk of bias which is concise but comprehensive. Also, compared to previous studies, we performed a much more comprehensive literature search which enabled us to include more studies for meta-analysis.

The potential mechanisms for acupuncture's beneficial clinical effects in treating the SCI have been studied in a large number of animal experiments. Electroacupuncture has been

shown to reduce glial fibrillary acidic protein levels in the injured cord,^{48, 49} which serves to inhibit reactive astrocyte proliferation. Electroacupuncture also has been shown to reduce epidermal growth factor receptor levels⁵⁰, and act as an antioxidant, anti-inflammation, and antiapoptosis agent thus promoting axonal regeneration, nerve growth factor improvement and some gene expressions which may also be linked to the neurological recovery of SCI⁵¹⁻⁵⁶. These effects can be postulated to reduce secondary spinal cord damage.

In conclusion, while this meta-analysis indicates that acupuncture is significantly associated with neurological recovery, improvement of motor function and functional abilities in SCI patients, the above limitations described make this effect questionable and a definitive conclusion difficult. We suggest that future investigators should be encouraged to pay special attention to safe-guards against bias with adequate monitoring and reporting of adverse events due to the acupuncture intervention. Special attention to accurate grading and scoring of neurological function must be given and studies should focus on acute injury with the intervention starting within 24 to 48 hours of injury.⁵⁷ Trials must include an accurate assessment of ASIA grade before the start of the trial, and use blinded assessment subsequently.⁵⁸ We also advocate standardizing the mode of acupuncture and recommend electroacupuncture be used consistently. Consequently, future trials should emphasise adequate training of researchers on the intervention as well as the clinical trial outcome measures of SCI and rigorous conduct based on guidelines such as international Standards and CONSORT statement or standards for reporting interventions in clinical trials of acupuncture (STRICTA).⁵⁹

Acknowledgement

RM conducted the search, abstracted the data and performed the statistical analysis. JC, XL and SD contributed to design, data acquisition and abstraction. SD and GM assisted in

statistical analysis. RM drafted the manuscript. All authors critically revised the manuscript and approved its final version.

This project is supported by National Natural Science Foundation of China (Grant No. 81102644), and Natural Science Foundation of Zhejiang province, China (Grant No. Y2100533); Training project of Human Resources for Health in Zhejiang Province, China (Zhejiang Health [2013] No.245) and Key Subject of tradition Chinese medicine of acupuncture ([2009] No. 30).

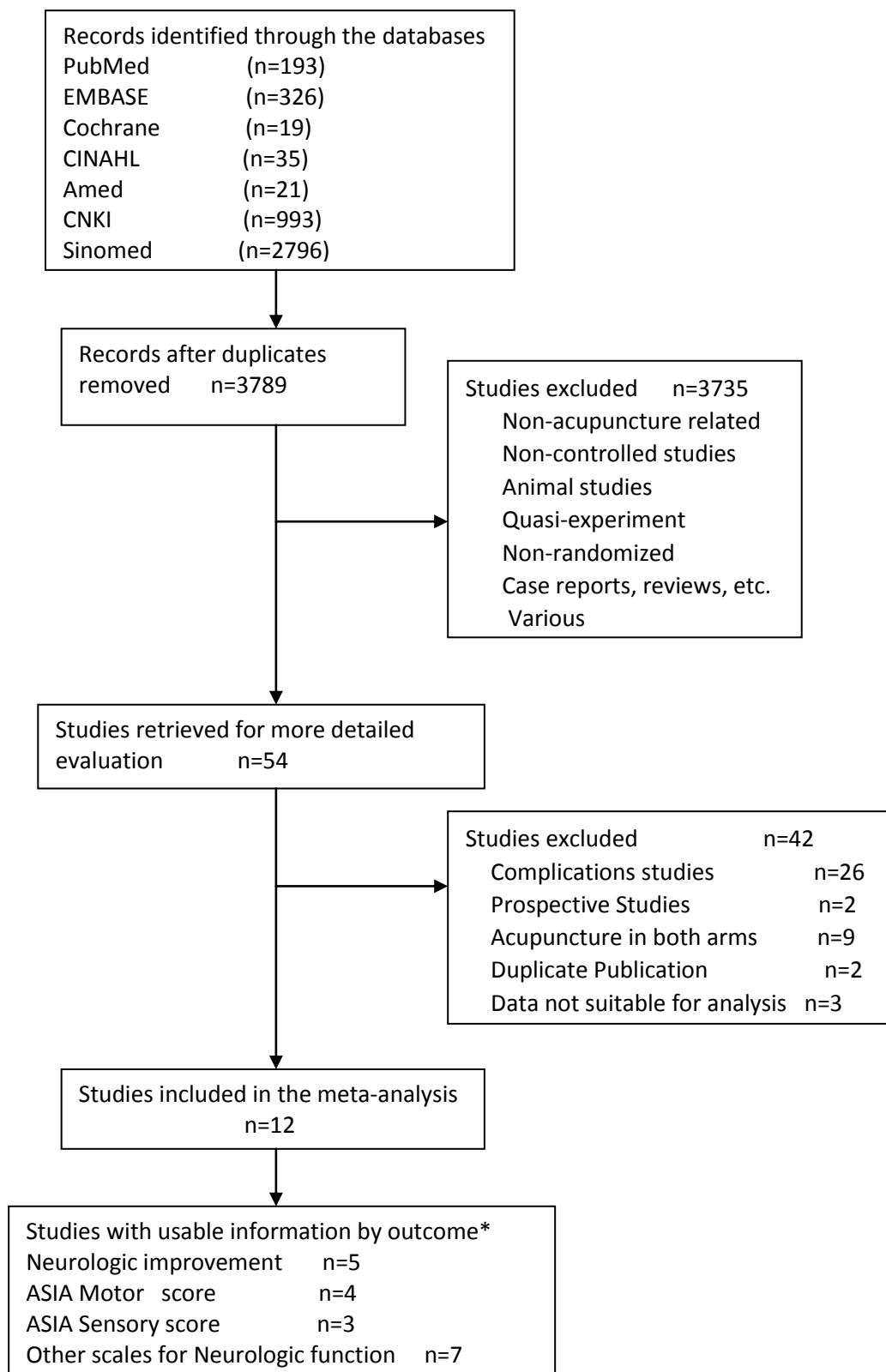
References

1. (2014). SpinalCord Injury Facts and Figures at a Glance. The National SCI Statistical Center: US.
2. O'Connor, P.J. (2005). Forecasting of spinal cord injury annual case numbers in Australia. *Arch Phys Med Rehabil* 86, 48-51.
3. Fawcett, J., Curt, A., Steeves, J., Coleman, W., Tuszynski, M., Lammertse, D., Bartlett, P., Blight, A., Dietz, V. and Ditunno, J. (2006). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal cord* 45, 190-205.
4. Walters, B.C., Hadley, M.N., Hurlbert, R.J., Aarabi, B., Dhall, S.S., Gelb, D.E., Harrigan, M.R., Rozelle, C.J., Ryken, T.C. and Theodore, N. (2013). Guidelines for the management of acute cervical spine and spinal cord injuries: 2013 update. *Neurosurgery* 60 Suppl 1, 82-91.
5. Taricco, M., Pagliacci, M.C., Telaro, E. and Adone, R. (2006). Pharmacological interventions for spasticity following spinal cord injury: results of a Cochrane systematic review. *Europa medicophysica* 42, 5-15.
6. Sipski, M.L. and Richards, J.S. (2006). Spinal cord injury rehabilitation: state of the science. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists* 85, 310-342.
7. Nayak, S., Shiflett, S.C., Schoenberger, N.E., Agostinelli, S., Kirshblum, S., Averill, A. and Cotter, A.C. (2001). Is acupuncture effective in treating chronic pain after spinal cord injury? *Arch Phys Med Rehabil* 82, 1578-1586.
8. Wong, A.M., Leong, C.P., Su, T.Y., Yu, S.W., Tsai, W.C. and Chen, C.P. (2003). Clinical trial of acupuncture for patients with spinal cord injuries. In: *American journal of physical medicine & rehabilitation*, pps. 21-27.
9. Dyson-Hudson, T.A., Kadar, P., LaFontaine, M., Emmons, R., Kirshblum, S.C., Tulskey, D. and Komaroff, E. (2007). Acupuncture for chronic shoulder pain in persons with spinal cord injury: a small-scale clinical trial. *Arch Phys Med Rehabil* 88, 1276-1283.
10. Shin, B.C., Lee, M.S., Kong, J.C., Jang, I. and Park, J.J. (2009). Acupuncture for spinal cord injury survivors in Chinese literature: a systematic review (Structured abstract). In: *Complementary Therapies in Medicine*, pps. 316-327.
11. Dorsher, P.T. and McIntosh, P.M. (2011). Acupuncture's Effects in Treating the Sequelae of Acute and Chronic Spinal Cord Injuries: A Review of Allopathic and Traditional Chinese Medicine Literature. *Evidence-based complementary and alternative medicine : eCAM* 2011, 428108.
12. Heo, I., Shin, B.C., Kim, Y.D., Hwang, E.H., Han, C.W. and Heo, K.H. (2013). Acupuncture for spinal cord injury and its complications: a systematic review and meta-analysis of randomized controlled trials. *Evidence-based complementary and alternative medicine : eCAM* 2013, 364216.

13. Wong, A.M., Leong, C.P., Su, T.Y., Yu, S.W., Tsai, W.C. and Chen, C.P. (2003). Clinical trial of acupuncture for patients with spinal cord injuries. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists* 82, 21-27.
14. Liu, J. and Hu, X.M. (2001). [Comparative study of therapeutic effects of acupuncture and chinese medical herbs for treatment of trauma paraplegia]. *Chinese Acupuncture & Moxibustion* 21, 3-5.
15. Xiao, H. and Wang, A.D. (2003). [Influence of acupuncture combined with rehabilitation training on ADL of spinal cord injury patients]. *Journal of New Chinese Medicine* 35, 46-47.
16. Guyatt, G.H., Oxman, A.D., Vist, G., Kunz, R., Brozek, J., Alonso-Coello, P., Montori, V., Akl, E.A., Djulbegovic, B., Falck-Ytter, Y., Norris, S.L., Williams, J.W., Jr., Atkins, D., Meerpohl, J. and Schunemann, H.J. (2011). GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). *Journal of clinical epidemiology* 64, 407-415.
17. Higgins, J.P., Altman, D.G., Gotzsche, P.C., Juni, P., Moher, D., Oxman, A.D., Savovic, J., Schulz, K.F., Weeks, L. and Sterne, J.A. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Clinical research ed.)* 343, d5928.
18. Waring, W.P., 3rd, Biering-Sorensen, F., Burns, S., Donovan, W., Graves, D., Jha, A., Jones, L., Kirshblum, S., Marino, R., Mulcahey, M.J., Reeves, R., Scelza, W.M., Schmidt-Read, M. and Stein, A. (2010). _ 2009 review and revisions of the international standards for the neurological classification of spinal cord injury. *J Spinal Cord Med* 33, 346-352.
19. Marino, R.J. and Graves, D.E. (2004). Metric properties of the ASIA motor score: subscales improve correlation with functional activities. *Arch Phys Med Rehabil* 85, 1804-1810.
20. Doi, S.A., Barendregt, J.J., Khan, S., Thalib, L. and Williams, G.M. (2015). Advances in the Meta-analysis of heterogeneous clinical trials I: The inverse variance heterogeneity model. *Contemporary clinical trials*.
21. Doi, S.A., Barendregt, J.J., Khan, S., Thalib, L. and Williams, G.M. (2015). Advances in the meta-analysis of heterogeneous clinical trials II: The quality effects model. *Contemporary clinical trials*.
22. Doi, S.A., Barendregt, J.J. and Mozurkewich, E.L. (2011). Meta-analysis of heterogeneous clinical trials: an empirical example. *Contemporary clinical trials* 32, 288-298.
23. Doi, S.A. and Thalib, L. (2008). A quality-effects model for meta-analysis. *Epidemiology (Cambridge, Mass.)* 19, 94-100.
24. Doi, S.A. and Thalib, L. (2009). An alternative quality adjustor for the quality effects model for meta-analysis. *Epidemiology (Cambridge, Mass.)* 20, 314.
25. Takkouche, B., Cadarso-Suarez, C. and Spiegelman, D. (1999). Evaluation of old and new tests of heterogeneity in epidemiologic meta-analysis. *American journal of epidemiology* 150, 206-215.
26. Doi, S.A.R. and Williams, G.M. (2013). *Methods of clinical epidemiology*. Springer: New York; Berlin.
27. Sterne, J.A., Egger, M. and Smith, G.D. (2001). Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis. *BMJ (Clinical research ed.)* 323, 101-105.
28. Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gotzsche, P.C., Ioannidis, J.P., Clarke, M., Devereaux, P.J., Kleijnen, J. and Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ (Clinical research ed.)* 339, b2700.
29. Egger, M., Davey Smith, G., Schneider, M. and Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ (Clinical research ed.)* 315, 629-634.

30. Chen, Z.G., Zhang, J.J., Wong, Z.M., Li, H.L. and Zhang, A.L. (1995). The clinical study of Governor vessel electroacupuncture treatment on the lower extremity spasticity in patients with spinal cord injury. *Journal of Clinical Acupuncture and Moxibustion* 11, 6-7.
31. Cui, X.M., Pan, X.M., Zhang, X.M., Deng, H.Z. and Yao, S.Y. (2004). [The rehabilitation function of electroacupuncture treatment in patients with traumatic spinal cord injury]. *Journal of Guangdong Medical College* 22, 170-171.
32. Chen, L.X., Duan, J.F., Zhan, X.R., Xie, Q. and Long, Q.H. (2005). [Electrical and auricular acupuncture for patients with acute spinal cord injury] *Chinese Journal of Rehabilitation Theory and Practice* 11, 934-935.
33. Gu, X.D., Yao, Y.H., Gu, M., Fu, J.M., Ren, Y. and Yin, H.K. (2005). [Clinical study on functional independence measure for patients with spinal cord injury of trauma treated by electroacupuncture] *Acupuncture Research* 30, 175-178.
34. Wang, J.L., Bai, T.Y. and Wang, X. (2010). [Observation on the efficacy of electroacupuncture plus rehabilitation training in treating spinal cord injury]. *Shanghai Journal of Acupuncture and Moxibustion* 29, 369-371.
35. Chen, J.Y. (2012). [The rehabilitation therapy and nursery for traumatic paraplegia patients treated by acupuncture combined with physical]. *China Modern Medicine* 19, 98-99.
36. Deng, C. and Lao, J.X. (2012). [Observation on the efficacy of jiaji electroacupuncture in treating incomplete spinal cord injury]. *Shanxi Journal of Traditional Chinese Medicine* 28, 30-31.
37. Wang, X.G., Guan, X. and Guo, Q.C. (2013). [Effect of acupuncture on trunk control ability and balance function in patients with spinal cord injury above lumber]. *Chinese Journal of Rehabilitation Theory and Practice* 19, 1180-1182.
38. Ye, S.L., Hang, H., Shen, D.T., Gu, J. and Zhang, X. (2014). [Clinical observation on jiaji points injection in treatment of traumatic spinal cord injury]. *Journal of Liaoning University of Traditional Chinese Medicine* 16, 116-118.
39. Brockwell, S.E. and Gordon, I.R. (2001). A comparison of statistical methods for meta-analysis. *Statistics in medicine* 20, 825-840.
40. Noma, H. (2011). Confidence intervals for a random-effects meta-analysis based on Bartlett-type corrections. *Statistics in medicine* 30, 3304-3312.
41. Scholten, R.J.P.M., de Beurs, E. and Bouter, L.M. (1999). From effect size into number needed to treat. *The Lancet* 354, 598.
42. Anderson, K.D., Acuff, M.E., Arp, B.G., Backus, D., Chun, S., Fisher, K., Fjerstad, J.E., Graves, D.E., Greenwald, K., Groah, S.L., Harkema, S.J., Horton, J.A., 3rd, Huang, M.N., Jennings, M., Kelley, K.S., Kessler, S.M., Kirshblum, S., Koltenuk, S., Linke, M., Ljungberg, I., Nagy, J., Nicolini, L., Roach, M.J., Salles, S., Scelza, W.M., Read, M.S., Reeves, R.K., Scott, M.D., Tansey, K.E., Theis, J.L., Tolfo, C.Z., Whitney, M., Williams, C.D., Winter, C.M. and Zanca, J.M. (2011). United States (US) multi-center study to assess the validity and reliability of the Spinal Cord Independence Measure (SCIM III). *Spinal Cord* 49, 880-885.
43. Tuszynski, M.H., Steeves, J.D., Fawcett, J.W., Lammertse, D., Kalichman, M., Rask, C., Curt, A., Ditunno, J.F., Fehlings, M.G., Guest, J.D., Ellaway, P.H., Kleitman, N., Bartlett, P.F., Blight, A.R., Dietz, V., Dobkin, B.H., Grossman, R. and Privat, A. (2007). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP Panel: clinical trial inclusion/exclusion criteria and ethics. *Spinal Cord* 45, 222-231.
44. Epstein, N.E. (2014). A review article on the benefits of early mobilization following spinal surgery and other medical/surgical procedures. *Surgical neurology international* 5, S66-73.
45. Weiss, D.J., Fried, G.W., Chancellor, M.B., Herbison, G.J., Ditunno, J.F., Jr. and Staas, W.E., Jr. (1996). Spinal cord injury and bladder recovery. *Arch Phys Med Rehabil* 77, 1133-1135.

46. Cardenas, D.D. and Jensen, M.P. (2006). Treatments for chronic pain in persons with spinal cord injury: A survey study. *J Spinal Cord Med* 29, 109-117.
47. van Hedel, H.J. and Curt, A. (2006). Fighting for each segment: estimating the clinical value of cervical and thoracic segments in SCI. *Journal of neurotrauma* 23, 1621-1631.
48. Yang, C., Li, B., Liu, T.S., Zhao, D.M. and Hu, F.A. (2005). [Effect of electroacupuncture on proliferation of astrocytes after spinal cord injury]. *Zhongguo zhen jiu = Chinese acupuncture & moxibustion* 25, 569-572.
49. Peng, B., Meng, X.F., Li, M., Luo, Y., Li, L.L., Zhang, J., Liu, X.C., Shi, J. and Chen, F. (2007). [Effects of electroacupuncture on the expression of epidermal growth factor receptor and glial fibrillary acidic protein after spinal cord injury in rats]. *Zhen ci yan jiu = Acupuncture research / [Zhongguo yi xue ke xue yuan Yi xue qing bao yan jiu suo bian ji]* 32, 219-223.
50. Wu, Y., Sun, Z., Li, Z., Zhao, Y. and Sun, S. (2002). Effect of acupuncture on free radicals in rats with early experimental spinal cord injury. *Journal of traditional Chinese medicine = Chung i tsa chih ying wen pan / sponsored by All-China Association of Traditional Chinese Medicine, Academy of Traditional Chinese Medicine* 22, 51-54.
51. Wang, X.Y., Li, X.L., Hong, S.Q., Xi-Yang, Y.B. and Wang, T.H. (2009). Electroacupuncture induced spinal plasticity is linked to multiple gene expressions in dorsal root deafferented rats. *Journal of molecular neuroscience : MN* 37, 97-110.
52. Ma, R.J., Zhang, L. and Wang, F.Y. (2003). [A review of the mechanisms of electroacupuncture treatment on spinal cord injury]. *Journal of Clinical Acupuncture and Moxibustion* 19, 52-55.
53. Ma, R.J., Zhang, L., Bai, J. and Gao, W.B. (2009). [Effects of electroacupuncture combining with herbs on expressions of GAP-43mRNA and BDNF mRNA in the rats with spinal cord injury]. *Chinese Archives of Traditional Chinese Medicine* 27, 576-578.
54. Ma, R.J., Zhang, L.J., Sun, L.Z., Nie, X.F., He, K.L. and ZhuC.H. (2014). [The study on OMgp expression of ASCI rats treated by Jia-Ji electroacupuncture]. *Chinese Archives of Traditional Chinese Medicine* 32, 1283-1286+1541.
55. Ma, R.J., Teng, X.Y., Zhang, L. and Gao, W.B. (2005). [Effects of electro-acupuncture on expressions of c-fos gene and brain-derived neurotrophic factor mRNA in the injured spinal cord in rats]. *Chinese Journal of Clinical Rehabilitation*, 114-116.
56. Jiang, S.H., Tu, W.Z., Zou, E.M., Hu, J., Wang, S., Li, J.R., Wang, W.S., He, R., Cheng, R.D. and Liao, W.J. (2014). Neuroprotective effects of different modalities of acupuncture on traumatic spinal cord injury in rats. *Evidence-based complementary and alternative medicine : eCAM* 2014, 431580.
57. Lammertse, D., Tuszynski, M.H., Steeves, J.D., Curt, A., Fawcett, J.W., Rask, C., Ditunno, J.F., Fehlings, M.G., Guest, J.D., Ellaway, P.H., Kleitman, N., Blight, A.R., Dobkin, B.H., Grossman, R., Katoh, H., Privat, A. and Kalichman, M. (2007). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: clinical trial design. *Spinal Cord* 45, 232-242.
58. Fawcett, J.W., Curt, A., Steeves, J.D., Coleman, W.P., Tuszynski, M.H., Lammertse, D., Bartlett, P.F., Blight, A.R., Dietz, V., Ditunno, J., Dobkin, B.H., Havton, L.A., Ellaway, P.H., Fehlings, M.G., Privat, A., Grossman, R., Guest, J.D., Kleitman, N., Nakamura, M., Gaviria, M. and Short, D. (2007). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord* 45, 190-205.
59. MacPherson, H., G.Altman, D., Hammerschlag, R., Li, X.P., Wu, T.X., White, A., Moher, D. and Liu, J.P. (2010). Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): Extending the CONSORT Statement. *Chinese Journal of Evidence-based Medicine* 10, 1228-1239.



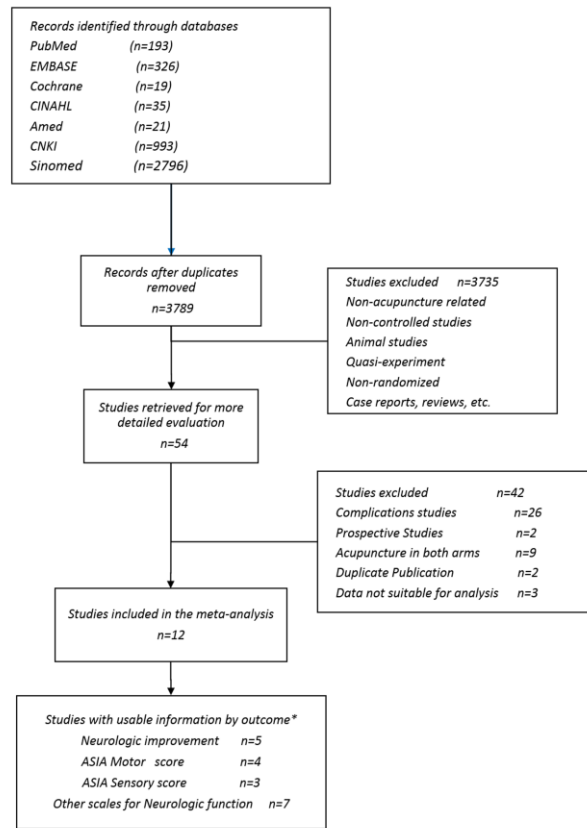
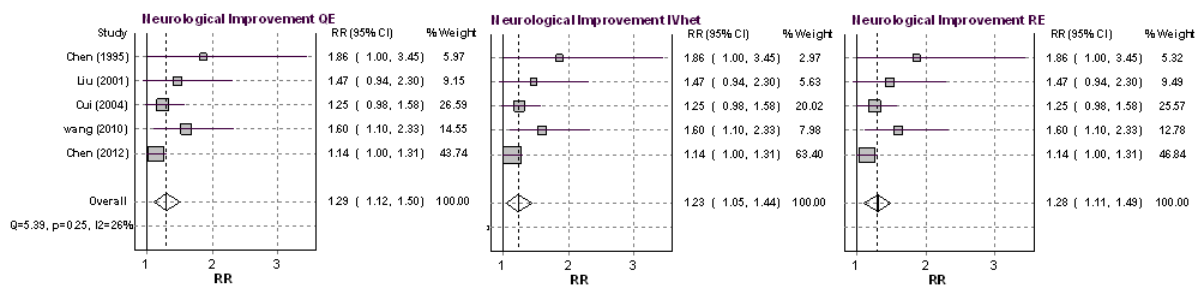


FIG. 1. Literature search flow-chart. (*Don't add to 12 because references that could fit into more than one outcome were categorized together and five of the twelve studies included more than one outcome measure suitable for meta-analysis.)



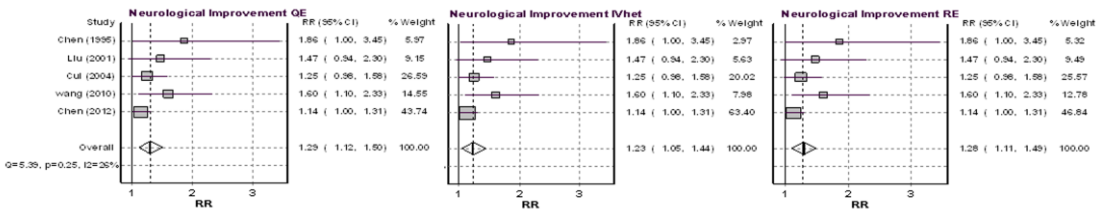
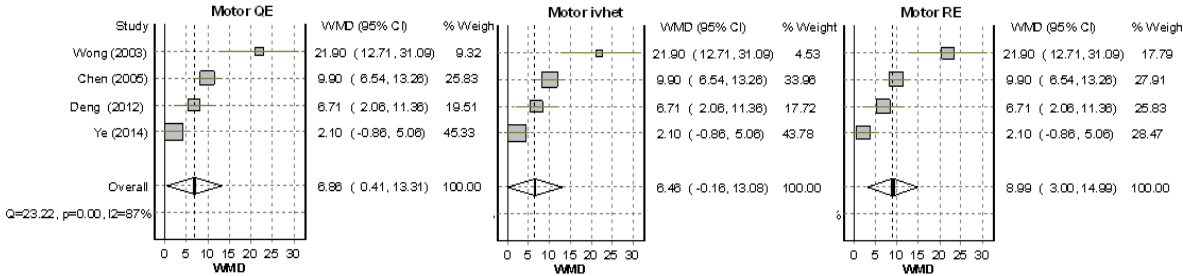


FIG.2. Forest plot of RRs for neurological improvement depicting the pooled estimates using the QE, IVhet and RE models.



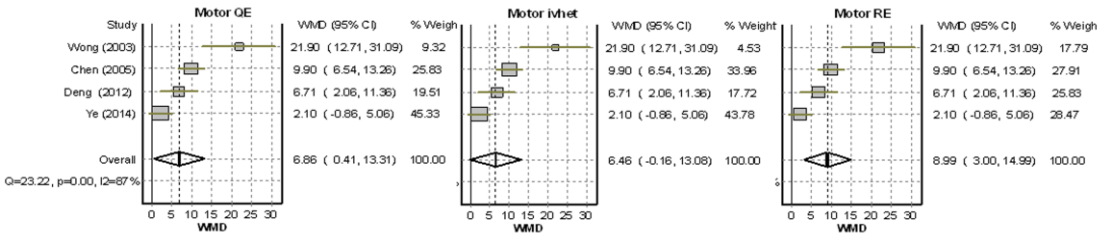
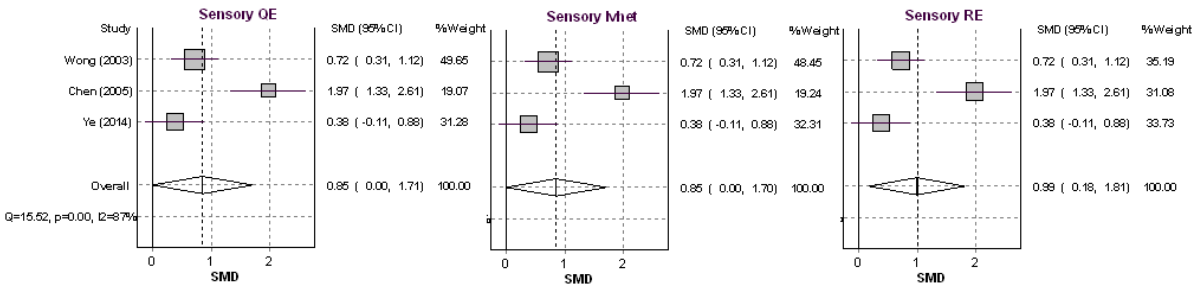


FIG.3. Forest plot of WMDs for motor recovery depicting the pooled estimates using the QE, IVhet and RE models.



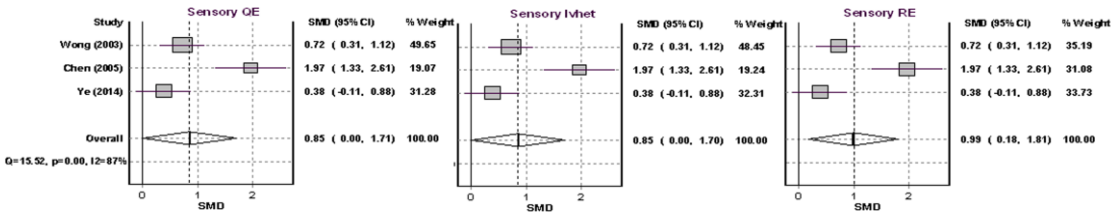
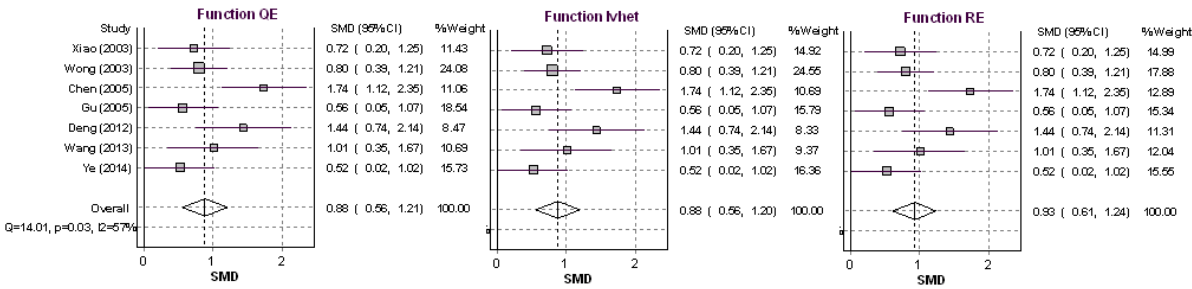


FIG.4. Forest plot of SMDs for sensory recovery depicting the pooled estimates using the QE, IVhet and RE models.



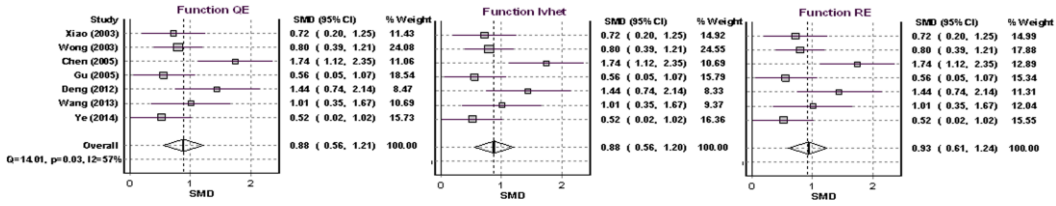
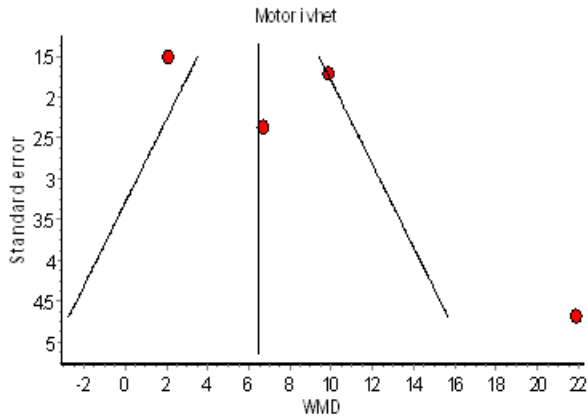
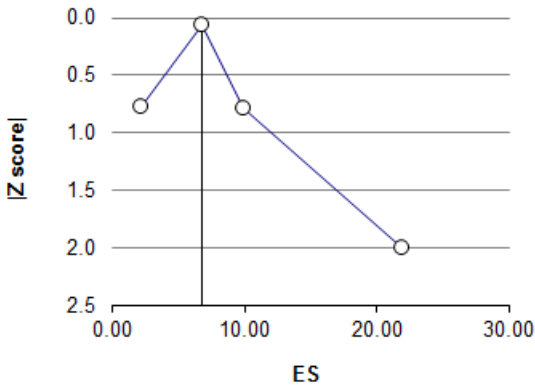
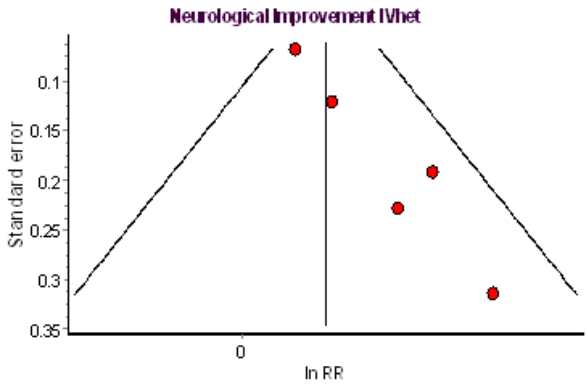
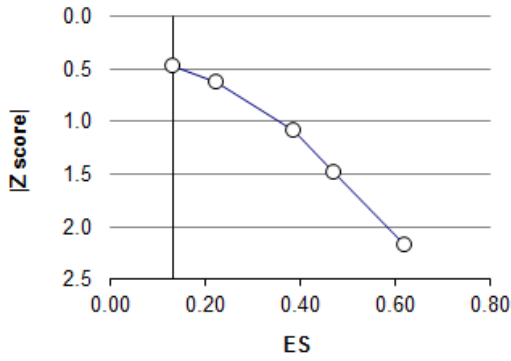
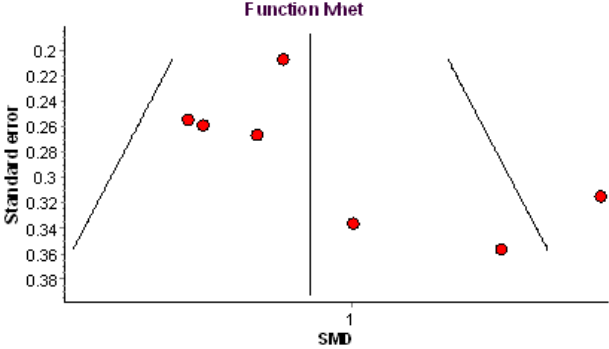
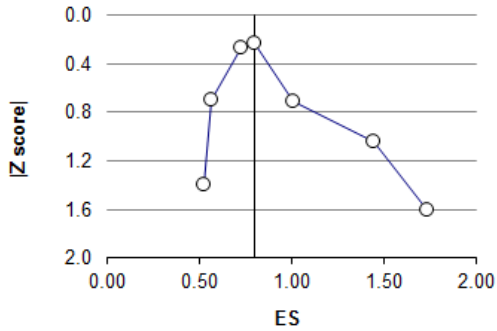


FIG.5. Forest plot of SMDs for functional ability recovery depicting the pooled estimates using the QE, IVhet and RE models.





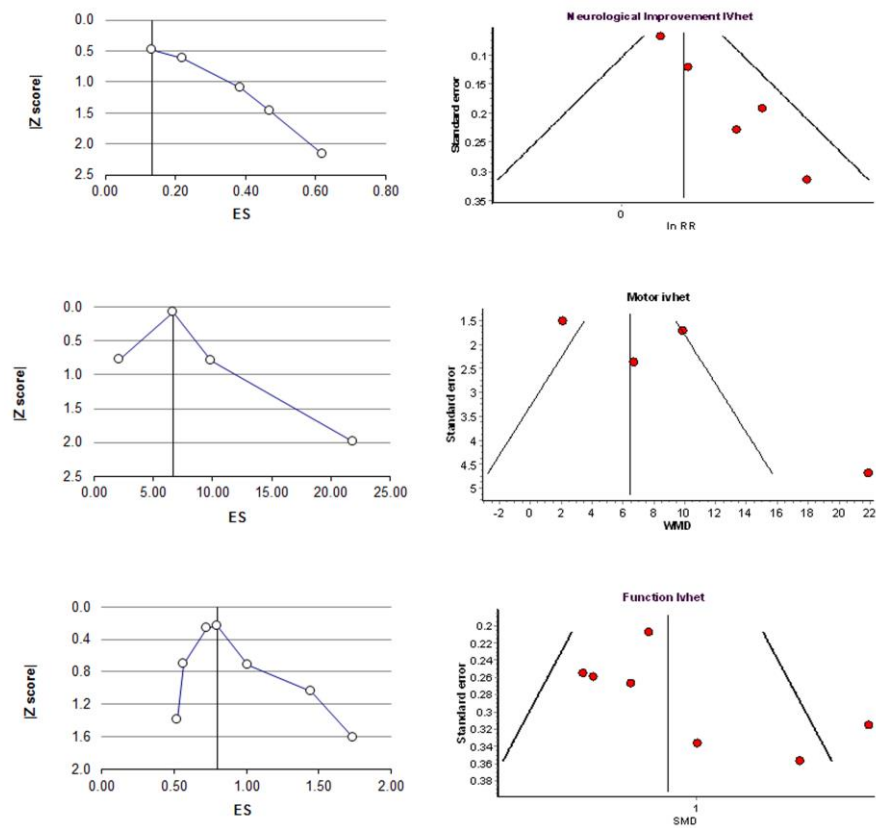


FIG.6. Doi (left) and Funnel plots (right) for the neurological improvement, motor recovery and functional ability recovery outcomes.

Table 1. Characteristic of Included Studies

Source	Study design	Included subjects (description including mean age, gender, type of injury, source of recruitment, eligibility)	Description of acupuncture intervention (A)	Description of control Intervention (B)
Chen (1995), Journal of Clinical Acupuncture and Moxibustion	RCT study with parallel 2 arms	Patients were recruited from the Rehabilitation Research Center of China (Beijing, China) inpatients from March 1989 to June 1994 and had a mean age of 34.16 ± 9.8 (range from 9 to 55) in acupuncture group while 34.06 ± 14.03 (range from 4 to 61) in the control group. There were 83.58% males and injury type was not recorded. The duration of SCI ranged from 1 to 81 months. Patients were included if they met the following eligibility criteria: lower extremity spasticity after SCI.	EA + R EA on upper and lower 1 point along the Governor vessel of the injured level (frequency is 1-2hz, one session is 30mins once a day, six times a week, total 48 treatments)	R PT rehabilitation, the specific method of exercise was not reported.
Liu (2001), Chinese acupuncture and moxibustion	RCT study with parallel 3 arms	Patients were recruited from the First Affiliated Hospital of Hunan College of Traditional Chinese Medicine (Changsha, China) inpatients and had a mean age of 36.25 ± 13.03 in acupuncture group while 34.15 ± 16.2 in the control group. There were 41.86% males and injury type was not recorded. The duration of SCI was 3.65 ± 2.45 months in acupuncture group while 3.44 ± 2.55 months in control group. Patients were included if they met the following eligibility criteria: incomplete traumatic spinal cord injury and complete paraplegia within 6 months.	EA EA were applied on the Governor vessel, nerve trunk and acupoint injection on back-shu points, front-mu points or common acupoint on limbs. Jiaji points were also used for injection with Chinese medicine injection, Vitamin B1 or Vitamin B12. Treatment was given for 6-18 months.	M TCM decoction depend on different stage of SCI

Wong (2003), Clinical trial of acupuncture for patients with spinal cord injuries	RCT study with parallel 2 arms, assessor blind	Patients were recruited from Chang Gung Memorial Hospital (Taiwan, China) inpatients and had a mean age of 35.1 ± 13.0 in acupuncture group while 34.7 ± 13.1 in control group. There were 70% males and injury type was traumatic. The duration of SCI was 58.6 ± 17.1 and 57.1 ± 18.7 days respectively in two groups. Patients were included if they were traumatic SCI with AIS is A or B. The exclusion criteria were: patients who required mechanical ventilation and those with concomitant traumatic brain injury, peripheral nerve injury, loss of consciousness, and multiple bony fractures. All patients gave informed consent to participate in the study.	EA+AA+R EA via the adhesive surface electrodes were applied to the bilateral Hou Hsi (SI3) and Shen Mo (B62). The frequency was set at 75 Hz, with pulse duration of 200 sec, and the magnitude of stimulation was set at 10 mV. Each session was 30 min and made of five sessions per week.	R Necessary rehabilitation therapies. The specific method of exercise is not reported.
Xiao (2003), Journal of New Chinese Medicine	RCT study with parallel 2 arms	Patients were recruited from Gansu Provincial Hospital of TCM and Gansu provincial hospital (Gansu, China) inpatients and had a mean age of 38.17 ± 10 in acupuncture group while 36.34 ± 10 in control group. There were 68.3% males and injury type was traumatic. Patients were included if they were traumatic SCI.	A+R Acupuncture on the jiaji points of 3 vertebrae above and 2 vertebrae below the injured vertebrae on the back while 3 cun above and 2 cun below CV8 of KI and ST meridian in the abdomen. Acupoints alternated every other day on the back and abdomen with the additional points on the limbs bilaterally. One session is 30 mins per day for 3 months treatments totally. (The specific session was not reported). Rehabilitation include Strength training, Wheelchair driver Training, transfer and gait training and Practical gait training et al.	M Medication of the basic treatment of bone fractures in all patients. One group was Energy mixture 500ml, qd ivgtt, for 15 days, continue another session after 5 days' rest. Another group was Safflower injection 20ml diluted, qd, ivgtt for 15 days; continue another session after 5 days' rest. The two groups were applied in alternatively for 3 sessions.

Cui (2004), Journal of Guangdong Medical College	RCT study with parallel 2 arms	Patients were recruited from the Affiliated Hospital of Guangdong Medical College inpatients and had a mean age of 34.50±12.23 in acupuncture group while 35.12±13.34 in the control group. The duration of SCI was 12.86±5.12 days in acupuncture group while 13.43±6.23 days in control group. There were 62.5% males and injury type was traumatic. The eligibility criteria were not reported.	EA + R Required points: upper limb contain Jiquan(HT1), Chize (LU5), Quze(PC3) and Shaohai (HT3); lower limb contain Chongmen (SP12), Yinmen (BL37), Huantiao (GB30), Weizhong (BL40), and stimulation point of peroneal nerve. Additional points could be selected on limbs and abdomen. The electrical points were selected among the acupoints above other than the points on abdomen, the wave was changed among different paralysis type. One session was 30min, once per day and 1 month treatment was one course. Total treatment was from 3 to 6 courses. R is the same as that in the control group.	R Conventional treatment, nursing care and function exercise. The specific treatment therapy was not reported.
Chen (2005), Chinese Journal of Rehabilitation Theory and Practice	RCT study with parallel 2 arms	Patients were recruited from General Hospital of Guangzhou Military Command (Guangdong, China) inpatients from JAN 1999 to MAY 2004 and had a mean age of 38.2±13.6 in acupuncture group while 37.6±12.8 in control group. The duration of their injury was not reported. There were 69.64% males and injury type was acute traumatic. Patients were included if they met the following eligibility criteria: The patients' injury was acute SCI, AIS was A or B. All the recruited patients received the necessary initial emergent care for SCI which included surgical bone fusions and fixations. The exclusion criteria were: patients who were receiving mechanical ventilation, those with traumatic brain injury, peripheral nerve injury, loss of consciousness and multiple bone fractures.	EA+ AA + R EA on bilateral Houxi (SI3) and Shenmai (BL62), once per day, each treatment session was 30min, six times a week. One course is for 3 months' treatments. Have a rest of 1 or 2 weeks between two courses. AA main points were AT3, AT4, TF4, AH6a and AH6, AH7 for additional choice. Alternately every other day on the two ears, for total 20-30 times treatments. R was the same as that in control group.	R Regular rehabilitation, specific exercise method was not reported.

Gu (2005), Acupuncture Research	RCT study with parallel 2 arms	Patients were recruited from Rehabilitation Medical Center of Jiaxing Second Hospital (Zhejiang, China) inpatients and had a mean age of 41.2 ± 8.2 in acupuncture group while 39.8 ± 7.6 in the control group. The duration of SCI was range from 7 to 365 days. There were 85.48% males and injury type was traumatic. Patients were included if they met the following eligibility criteria: definite SCI diagnosed by MRI.	EA + R EA on Jianyu (LI15), Quchi (LI11), Waiguan (TE5), etc. Each treatment session was 30min, once per day, The frequency was set at 60hz, wave is continuous and the magnitude of stimulation was set at 3-5V R was the same as that in control group.	R Kinesitherapy and occupational therapy. Rehabilitation program was the following steps: Lying - a bed of transferring - a seat - a seat in a position balance in three grade - standing - stand balanced in three grade - walking. Oral drugs was Methycobal, 50ug, tid.
Wang(2010), Shanghai Journal of Acupuncture and Moxibustion	RCT study with parallel 2 arms	Patients were recruited from Shandong Jiaotong Hospital (Shandong, China) inpatients from 1998 to 2009. There was no statistical significance in patients' mean age, gender, duration, level and severity of injury as description but the specific data was not reported in the literature. Patients were included if they met the following eligibility criteria: paralysis of limbs, urinary and fecal incontinence and losing the function of movement and sensory. Spinal cord injury was detected by CT. The exclusion criteria were not reported.	EA + R + M Acupoints were the points on the Governor vessel (1 or 2 spinal processes above and lower of the injured level) and Jiaji points. Upper limb points were Jianyu (LI15), Quchi (LI11), Waiguan (TE5), Hegu (LI4), Houxi (SI3); Lower limb points were Huantiao (GB30), Fengshi (GB31), Yanglingquan (GB34), Zusanli (ST36), Sanyinjiao (SP6), Taixi (KI3), Taichong (LR3). Guanyuan (CV4), Qihai (CV6), Qugu (CV2) were used for urine incontinence, while Tianshu (ST25), Zhigou (TE6), Dachangshu (BL25) used for fecal incontinence. EA was applied on acupoints on Governor vessel and GB31, GB32, ST36, BL36, ST40. The frequency was 20Hz. One session was 30mins once a day and 10 days was a course. Have a rest of 5 days	R + M R is to apply different kinds of PT and OT twice a day, 10 days is a course. Have a rest between 2 courses. Medication was neurotrophic drugs; steroid and symptomatic treatment for patients' specific situation.

			between 2 courses. Total treatment is for 6 months. R and M was the same as that in control group.	
Chen (2012), China Modern Medicine	RCT study with parallel 2 arms assessor blind	Patients were recruited from the Eighth Hospital of Changsha City (Hunan, China) inpatients from JAN 2010 to JUN 2012 and patient's age was from 28-70. The duration of SCI was more than 4 weeks. There were 54.0% males and injury type was not reported. Patients were included if they met the following eligibility criteria: traumatic injury with sensory disorder and urinary and fecal incontinence.	A + R Acupuncture on the Governor vessel, Nerve trunk stimulation, back-Shu and front-Mu points, general points or jiaji points. Low-frequency stimulation on the muscles was also used. R is the same as that in control group.	R Conventional medications and nursing care (psychological nursing, rehabilitation exercises and puncture nursing).
Deng (2012), Shanxi Journal of Traditional Chinese Medicine	RCT study with parallel 2 arms	Patients were recruited from Foshan Hospital of TCM inpatients (Guangdong, china) from MAR 2009 to JAN 2011 and the patient's age was from 21 to 60. The duration of SCI was 0-6 months. There were 57.5% males and injury type was traumatic. Patients were included if they met the following eligibility criteria: corresponding to the thoracolumbar fractures diagnosis standard, AIS was C or D and injured segment was T9 or T10 or T11 or T12 or L1. The age of patients was between 18 and 60.	EA + M EA on Jiaji points and Bilateral points were selected on limbs as Zhibian(BL54),Huantiao(GB30), Biguan(ST31), Yangli ngquan(GB34), Futu(ST32), Zusanli(ST36), Kunlun (BL60) Each session was 30 min, once per day, 5 times a week, total of 8 weeks. M was the same as that in control group.	M Monosialotetrahexosylg anglioside (GM1) 20mg, qd, ivgtt, for 8 weeks.

Wang (2013), Chinese Journal of Rehabilitation Theory and Practice	RCT study with parallel 2 arms	Patients were recruited from the First Affiliated Hospital of Henan University of TCM (Henan, China) inpatients from Jan 2011 to Aug 2012 and had a mean age of 37.3 ± 7.35 in acupuncture group while 35.8 ± 6.3 in the control group. The duration of SCI was 148 ± 13.8 days in acupuncture group and 151.3 ± 12.5 days in control group. Injury type was traumatic and gender was not reported. Patients were included if they met the following eligibility criteria: traumatic injury corresponding to the criteria of ASIA 2000 in clinical diagnosis, all patients signed informed consent to participate in the study. The exclusion criteria were high blood pressure out of control, severe heart and lung disease, severe orthostatic hypotension, deep vein thrombosis, severe osteoporosis; severe pressure sores and cognitive dysfunction.	A + R Acupoints selected depended on different injury segment which were mainly on the trunk (strong stimulation rotating manipulation, manipulate it in every five minutes) Each session was 30 mins, once per day, 6 times a week. Total was 8 weeks. R was the same as that in control group.	R Limb joint training method by Nustep T4 and accessory movement, 11 times a week for 8 weeks.
Ye (2014), Journal of Liaoning University of Traditional Chinese Medicine	RCT study with parallel 2 arms	Patients were recruited from Guangzhou General Hospital of Guangzhou Military Command (Guangdong, China) inpatients and had a mean age of was 33.46 ± 10.62 in acupuncture group while 35.14 ± 11.31 in control group. There were 59.375% males and injury type was traumatic. The duration of SCI ranged from 3 to 5.5 months in acupuncture group and 2.8 to 6.5 months in control group. Patients were included if they were traumatic injury and condition was relatively stable after given spinal internal fixation surgery. Complete SCI and incomplete SCI were both included.	A + R + M Jiaji points injection on upper and lower 2 point along the Governor meridian of the injured level. Mecobalamin injection was used for 2 points a day, every point's injection 1ml, injection in turn. R and M was the same as that in control group.	R + M R : OT, PT and ADL training, once a day, 5 days treatment continuously, have a rest for 2days, then go on treatment. 2 months treatments as a course. Medication was neurotrophic drugs, steroid and symptomatic treatment for patients' specific situation.

RCT, randomized controlled trial; A, acupuncture; EA, electroacupuncture; AA, auricular acupuncture; R, rehabilitation; M, medication

Duration of injury is the time after SCI if it is unspecified.

h: hour(s); T, tetraplegia; P, paraplegia; I, incomplete; C, complete; NEU, neurological; NR, not reported; NA, not applicable.

Table 2 Characteristics of SCI Level, SCI Severity And Duration of Follow-Up of included studies

Source	SCI level (patients: n/total)	SCI severity (as measured in the study by baseline scores Mean(SD), acupuncture/control)	Duration of follow-up
Chen(1995), Journal of Clinical Acupuncture and Moxibustion	C : Acupuncture: 11/32 Control: 32/35 T : Acupuncture: 19/32 Control: 10/35 L : Acupuncture:2/32	Ashworth scale Acupuncture: 2 (0.15)/Control: 1.5 (0.10)	6 months
Liu (2001), Chinese acupuncture and moxibustion	C5-T10: Acupuncture: 3/17 Control: 2/15 C11-L5: Acupuncture: 14/17 Control: 13/15	Frankel scale for incomplete SCI, Mean (SD) was not reported.	6-18 months

Wong (2003), Clinical trial of acupuncture for patients with spinal cord injuries	Quadriplegia: Acupuncture: 19/50 Control: 18/50 Paraplegia: Acupuncture: 31/50 Control: 32/50	ASIA motor scores Acupuncture: 41 (21.5)/Control: 41 (17.7) ASIA PP sensory scores Acupuncture: 60.8 (27.7)/ Control: 59.1(24.9) ASIA LT sensory scores Acupuncture: 63 (23.2)/Control: 60.8 (24.4) FIM total score Acupuncture: 49.9 (13.1)/Control: 47.7 (12.3) AIS was A or B	1-yr post injury follow-up
Xiao (2003), Journal of New Chinese Medicine	Quadriplegia: Acupuncture: 6/30 Control: 24/30 Paraplegia: Acupuncture: 5/30 Control: 25/30	Barthel index score: Acupuncture: 40.35(24.33)/Control: 39.09(24.72)	3 months
Cui (2004), Journal of Guangdong Medical College	C4-C7: Acupuncture: 20/37 Control: 18/35 T1-L4: Acupuncture: 17/37 Control: 17/37	FIM(Complete independent rate)	3-6 months
Chen (2005), Chinese Journal of Rehabilitation Theory and Practice	N.R.	AIS was A or B The baseline of ASIA and FIM score was not reported.	1-yr post injury
Gu (2005), Acupuncture Research	C: Acupuncture: 2/32 Control: 4/30 T: Acupuncture: 26/32 Control: 24/30 L: Acupuncture: 2/32 Control: 4/30	AIS was A or B or C or D. Total FIM score Acupuncture: 42.69(15.62)/ Control: 40.92(16.44)	6 months
Wang (2010), Shanghai Journal of Acupuncture and Moxibustion	N.R.	Function grade of limb (baseline was not reported)	60 days

Chen (2012), China Modern Medicine	paraplegia	N.R.	N.R.
Deng (2012), Shanxi Journal of Traditional Chinese Medicine	T9-L1, number of different level was not reported	AIS were C or D. ASIA Muscle index Acupuncture: 66.12(5.02)/ Control: 66.23(6.19) Walking index for SCI Acupuncture: 0/ Control: 0 ADL Acupuncture: 30.17(2.80)/ Control: 30.22(2.53)	8 weeks
Wang (2013), Chinese Journal of Rehabilitation Theory and Practice	C: Acupuncture: 1/20 Control: 0/20 T: Acupuncture: 19/20 Control: 20/20	AIS were B, C or D. Fugl-meyer Acupuncture: 1.76(1.08)/Control: 1.28(1.05)	8 weeks
Ye (2014), Journal of Liaoning University of Traditional Chinese Medicine	T: 30 L: 34	ADL Acupuncture: 37.43(11.50)/Control: 42.15(14.52) ASIA motor Acupuncture: 15.1(5.2)/Control: 14.3(4.9) ASIA LT sensory Acupuncture: 7.2(2.9)/Control: 6.8(3.3) ASIA PP sensory Acupuncture: 10.7(3.42)/Control: 11.1(4.22)	4 months

C, cervical; T, thoracic; L, lumbar; S, sacral; AIS, American Spinal Injury Association Impairment Scale; ASIA, American Spinal Injury Association; FIM, Functional Independence Measure; ADL, Activities of daily living; LT, light touch; PP, pin prick; NR, not reported;

Table 3. A Tailored Checklist for Assessing the Susceptibility to Bias in Therapeutic Comparative Studies for Spinal Cord Injury(Liu-Doi scale)

Item	Questions	Score
		1=Yes/Not applicable, 0=No/Unclear
	Design bias	
1	<p>What was the type of design?</p> <p>a) randomized and allocation concealed – 3 points</p> <p>b) randomized only – 2 points</p> <p>c) prospective cohort – 1 point</p> <p>d) retrospective cohort or case control – 0 point</p> <p>[note of b): 1. Was the study described as randomized (this includes words such as randomly, random, and randomization)? Yes=1, No=0</p> <p>2. Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc)? Yes=1, No=0]</p>	
2	Was the duration of active treatment appropriate for the demonstration of study outcome (e.g. ≥ 6 months for neurological recovery of SCI)*?	
	Selection bias	
3	Did the inclusion/exclusion criteria remain consistent across the comparison groups of the study?	
4	Was the strategy for recruitment into the study the same across comparison groups (e.g. not from same populations or both groups were not recruited over the same time period)?	
5	Was the interval between the start of intervention and outcome the same across comparison groups, or if different, were appropriate analyses used to equalize this (e.g. time-to-event analyses)?	
6	Was attrition $< 20\%$, or if not, was follow-up done for these subjects to ensure their loss was not related to outcome?	
	Information bias	
7	Were the outcomes of interest in the study pre-specified?	

8	Were reproducible measures (clear name of predefined scale or clear details of non-predefined scale were presented) of study outcomes implemented in the same way across comparison groups?	
9	Were the outcome assessors blinded to the nature of intervention or control?	
10	Were the subjects blinded to the nature of intervention or control ?	
11	Apart from blinding, were any other safeguards described and used for assuring the reliability of study outcomes?	
12	Were data assessed and recorded in the same way for both comparison groups and across time points?	
13	Were interventions/exposures clearly defined (all essential components were described) and implemented in the same way across both study groups?	
	Confounding bias	
14	Were the groups similar at baseline in key confounding variables or if not were steps taken to achieve comparability of key confounders (e.g. through matching, stratification, interaction terms, multivariate analysis, or other statistical adjustment such as instrumental variables)? a) age ; b) duration of disease; c) level of lesion; d) severity of SCI ; e) gender	
	Analytical bias	
15	Were effect sizes based on the data available at post assessment or pre-defined subgroups rather than a post hoc portion of the data?	
16	Was intention-to-treat analyses conducted for the outcome of interest?	
17	Were all data available (i.e. they did not need to be estimated from results)?	

The total quality score ranges from 0 to 23 points. SCI: spinal cord injury.

Table 4. Sensitivity analysis for the functional recovery outcome

Studies selected if		QE Model(95% CI) SMD	IVhet Model(95% CI) SMD	RE Model(95% CI) SMD	I-squared
Publication year					
<2006	n=4	0.88 (0.42, 1.34)	0.88 (0.42, 1.34)	0.92 (0.48, 1.37)	67.96
>=2006	n=3	0.88 (0.33, 1.43)	0.88 (0.33, 1.43)	0.95 (0.40, 1.49)	56.96
Study sample size					
<30	n=3	1.40 (0.97, 1.82)	1.41 (0.98, 1.83)	1.41 (0.98, 1.83)	20.13
>=30	n=4	0.66 (0.42, 0.90)	0.67 (0.43, 0.91)	0.67 (0.43, 0.91)	0.00
Duration of disease					
Acute	n=2	1.07 (0.10, 2.04)	1.08 (0.12, 2.05)	1.41 (0.98, 1.83)	83.75
Not acute	n=2	0.71 (0.24, 1.18)	0.70 (0.23, 1.17)	0.71 (0.24, 1.18)	25.48
Severity of injury					
Include Grade A	n=3	0.91 (0.27, 1.54)	0.92 (0.28, 1.56)	1.00 (0.39, 1.62)	77.62
Not include Grade A	n=2	1.20 (0.72, 1.68)	1.21 (0.73, 1.69)	1.21 (0.73, 1.69)	0.00
Control group intervention					
Rehabilitation controls	n=5	0.84 (0.44, 1.24)	0.85 (0.44, 1.25)	1.04 (0.34, 1.75)	63.95
other controls	n=2	1.02 (0.32, 1.72)	0.98 (0.27, 1.69)	1.04 (0.34, 1.75)	0.00
Sessions given					
Fixed session	n=4	0.85 (0.47, 1.22)	0.83 (0.46, 1.21)	0.87 (0.49, 1.24)	38.58
Varying session	n=2	1.07 (0.10, 2.04)	1.08 (0.12, 2.05)	1.24 (0.32, 2.15)	83.75
Type of outcome scale					
FIM scale	n=3	0.91 (0.27, 1.54)	0.92 (0.28, 1.56)	1.00 (0.39, 1.62)	77.62
Other scale	n=4	0.85 (0.47, 1.22)	0.83 (0.46, 1.21)	0.87 (0.49, 1.24)	38.58

SMD, standardized mean difference; QE, quality effects; IVhet, inverse variance heterogeneity; RE, random effects.

